



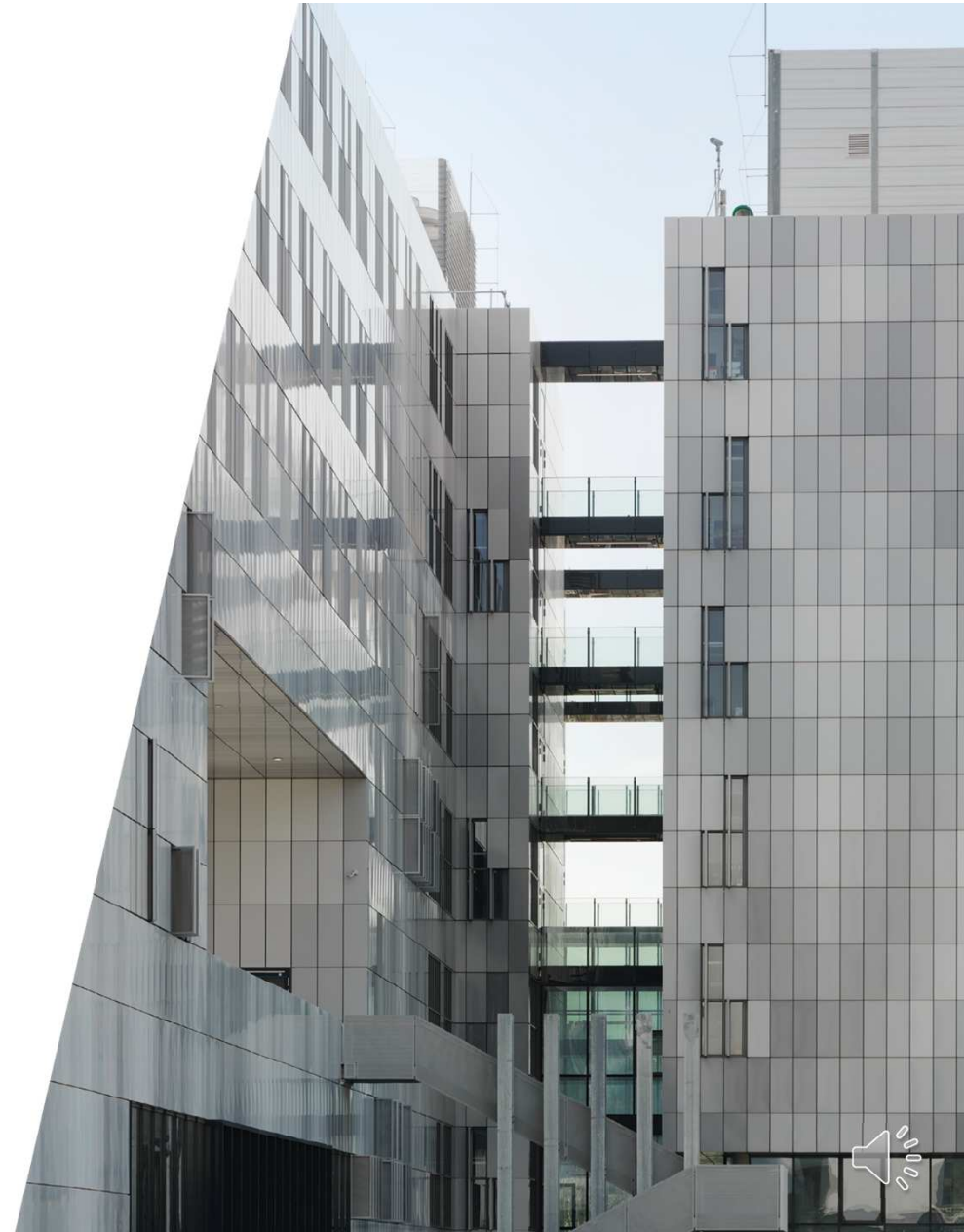
Medical University of Graz

# UPPER GI TRACT CASE #1

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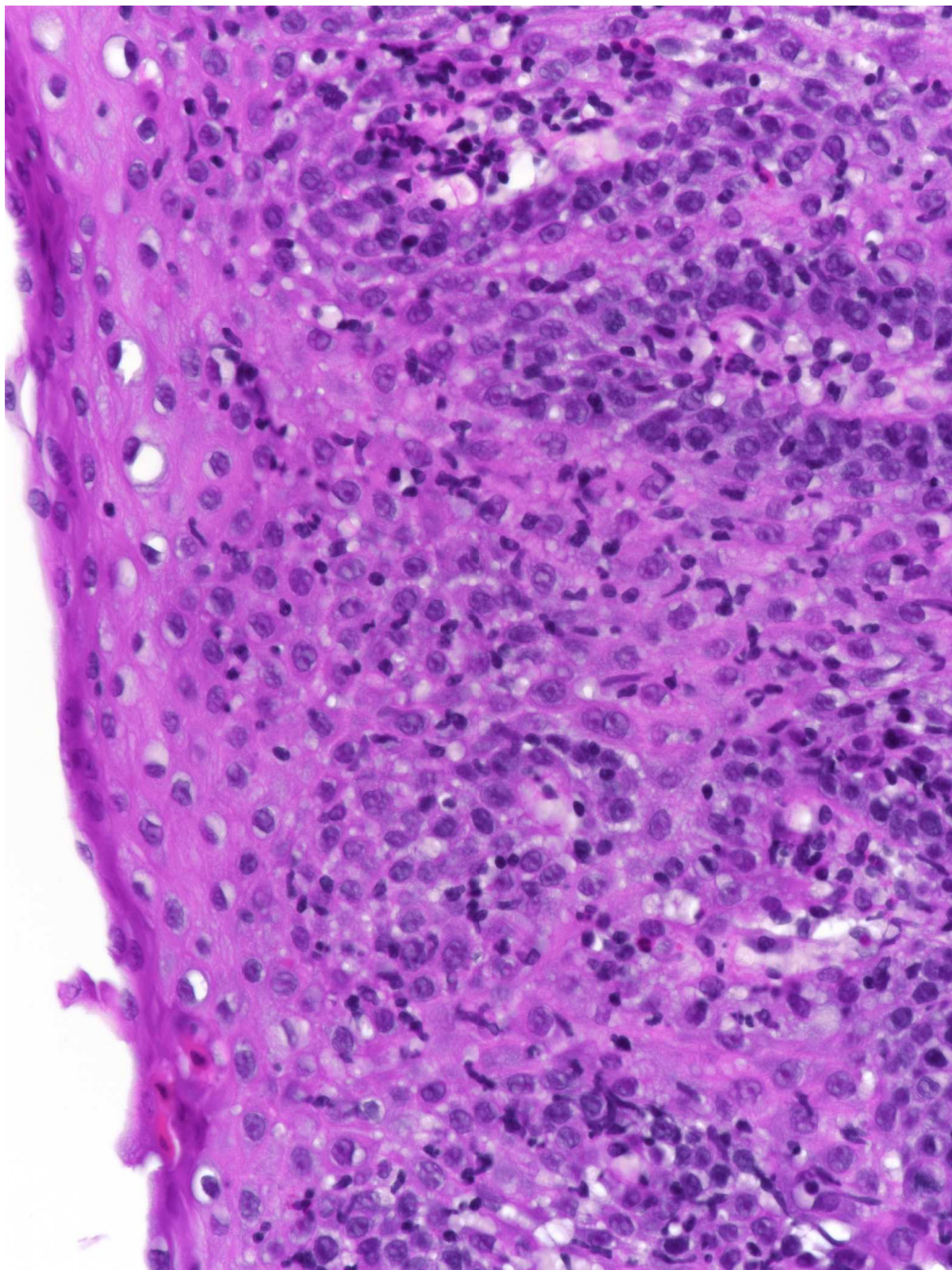
# Background story

- ▶ 82-year-old female
- ▶ Clinical symptoms: dysphagia
- ▶ Endoscopy: severe oesophagitis
- ▶ Pathology request form:
  - ▶ Viral oesophagitis?
  - ▶ Eosinophilic oesophagitis?
- ▶ Biopsies from different parts of the oesophagus

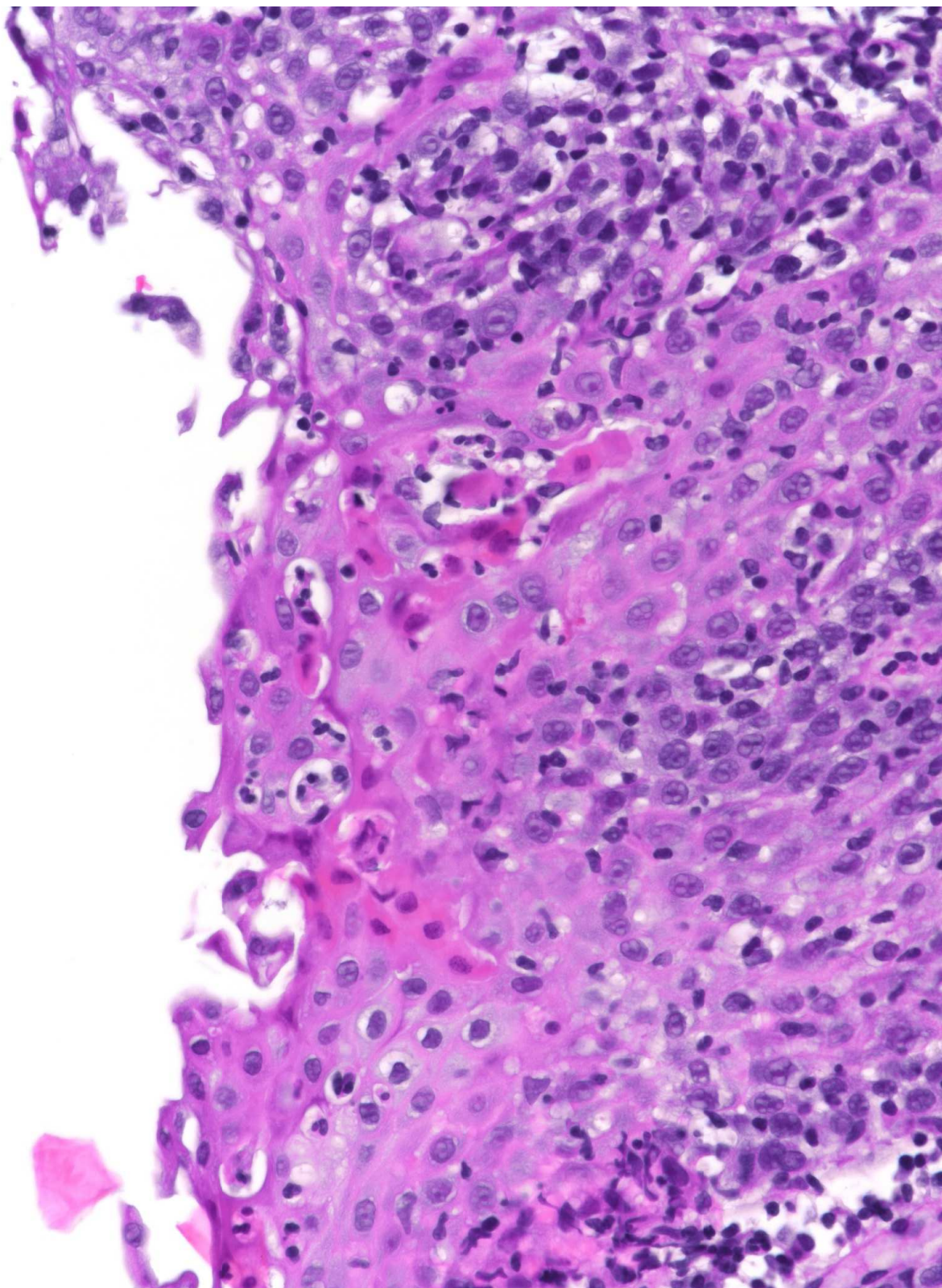




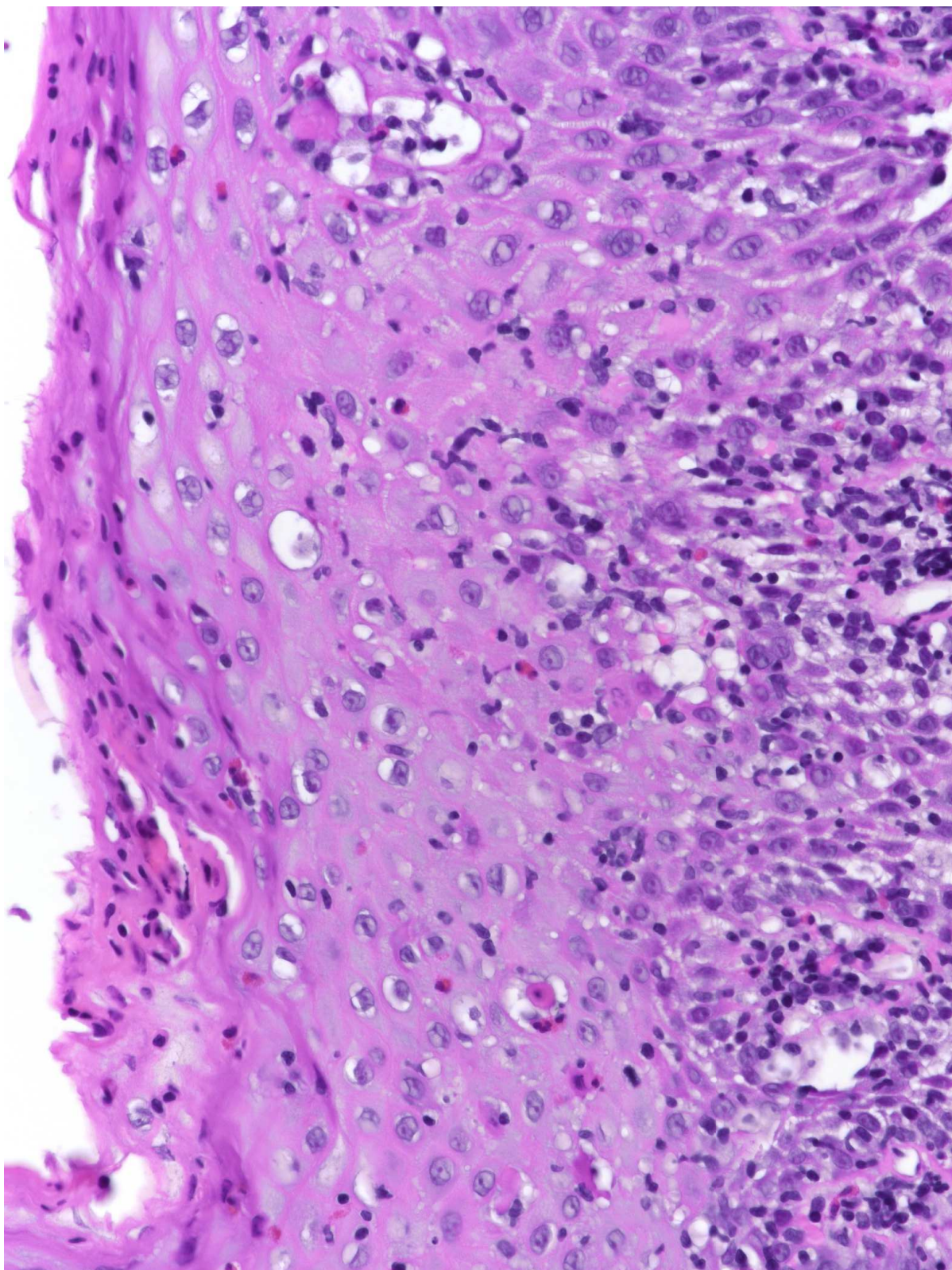




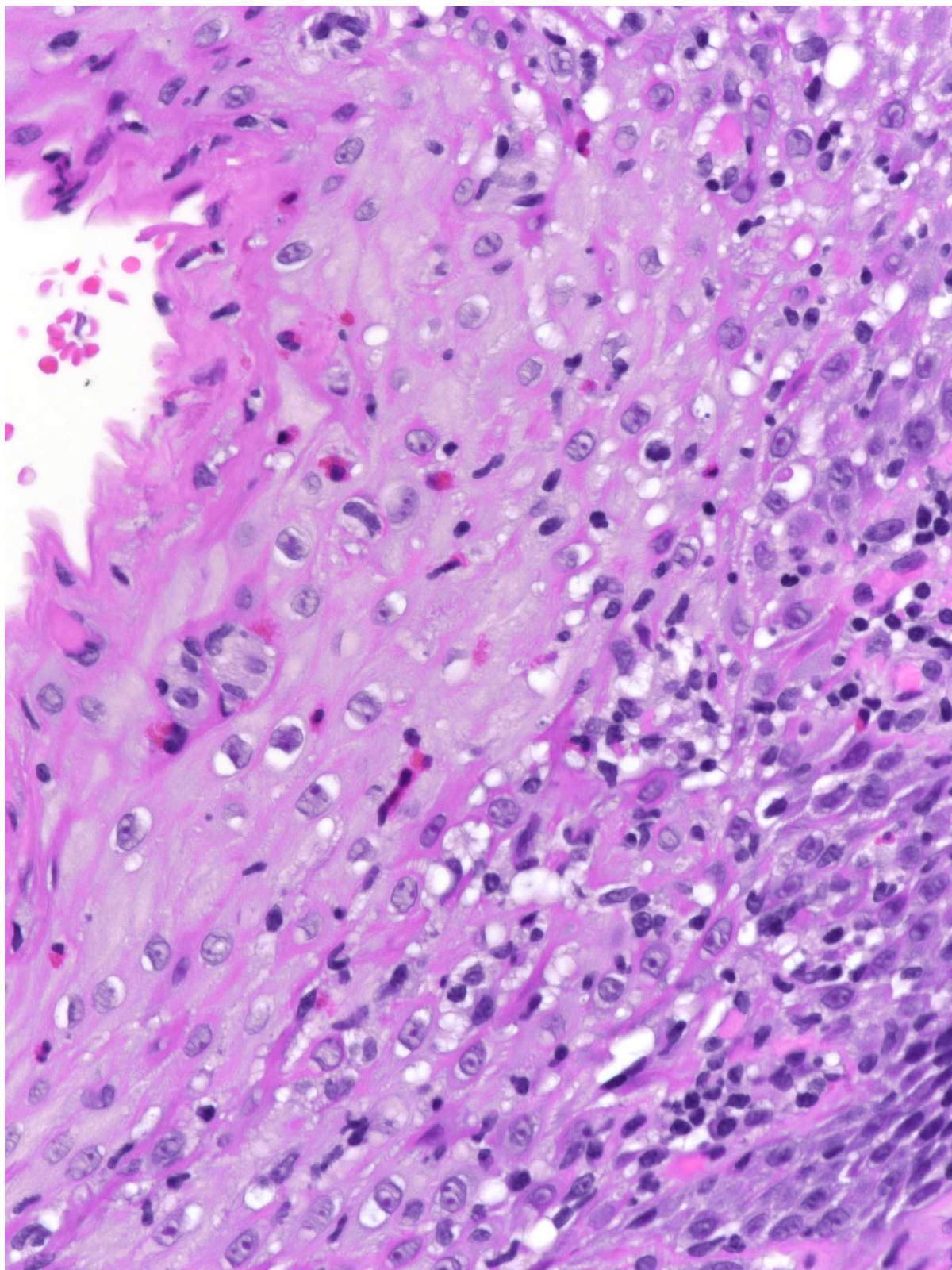




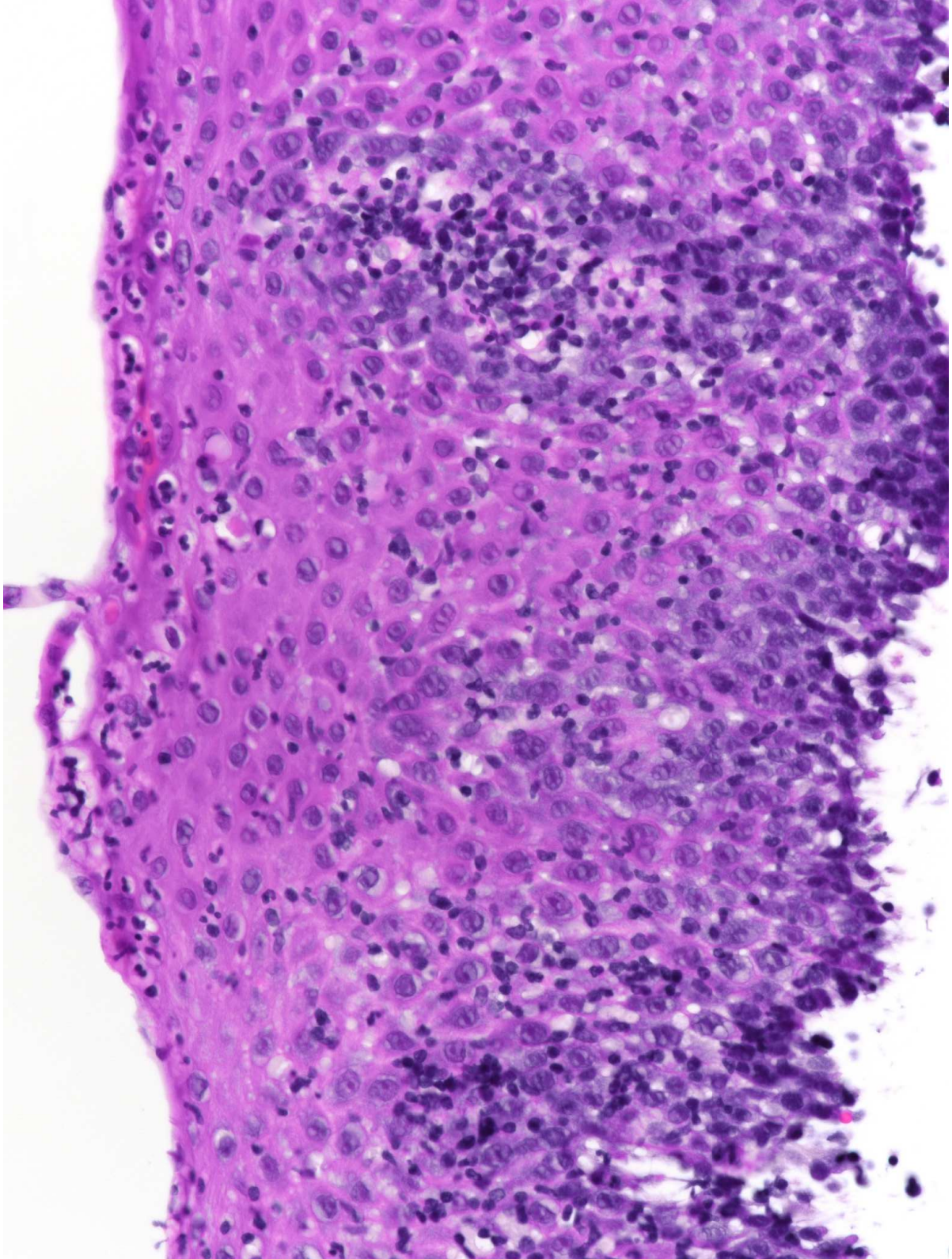














# What is your diagnosis?

- ▶ Viral oesophagitis
- ▶ Eosinophilic oesophagitis
- ▶ Lymphocytic oesophagitis
- ▶ Pill's oesophagitis
- ▶ Extranodal marginal zone B-NHL (MALT lymphoma)
- ▶ None of the above

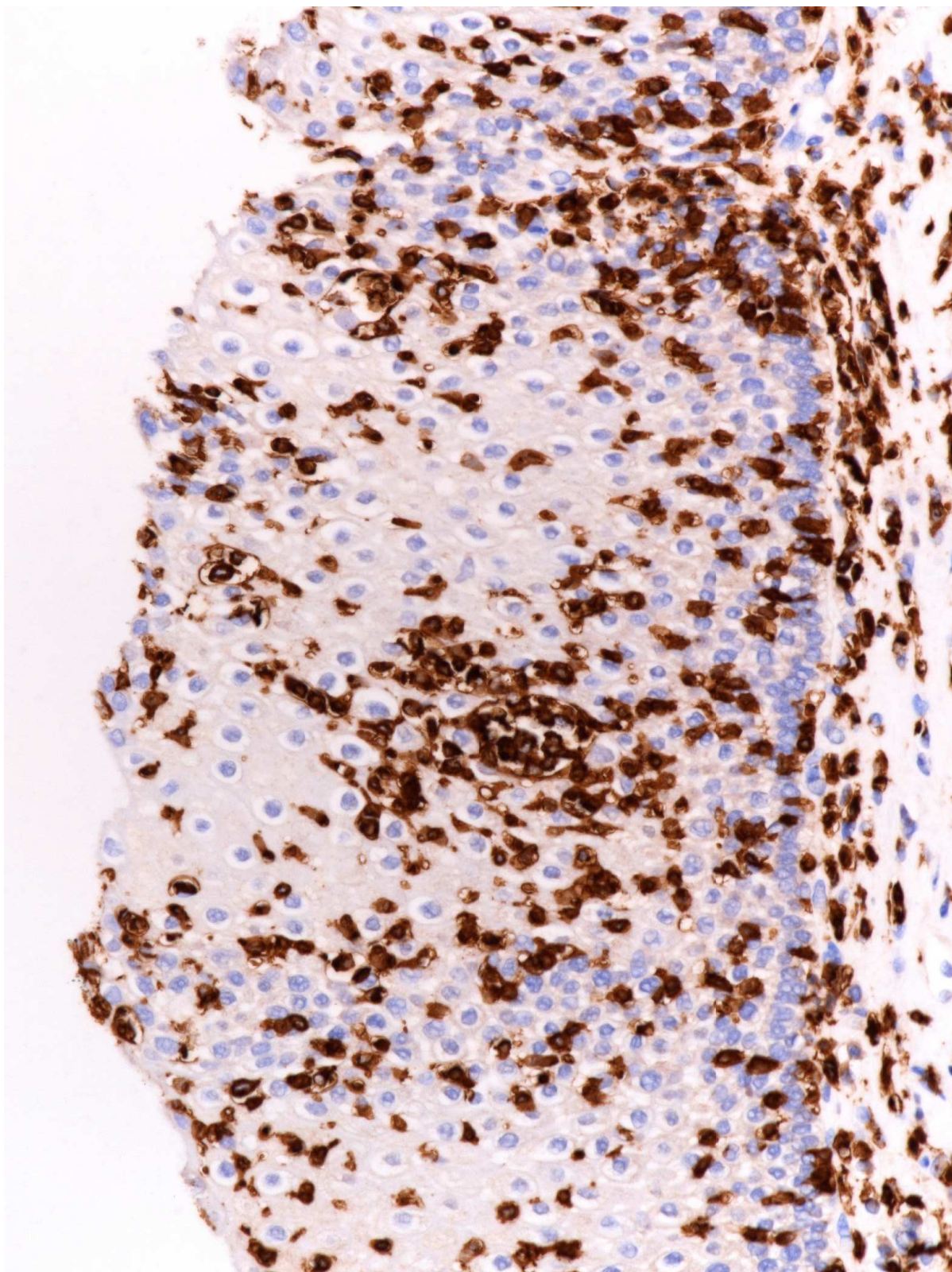


# Would you like to see extra stains?

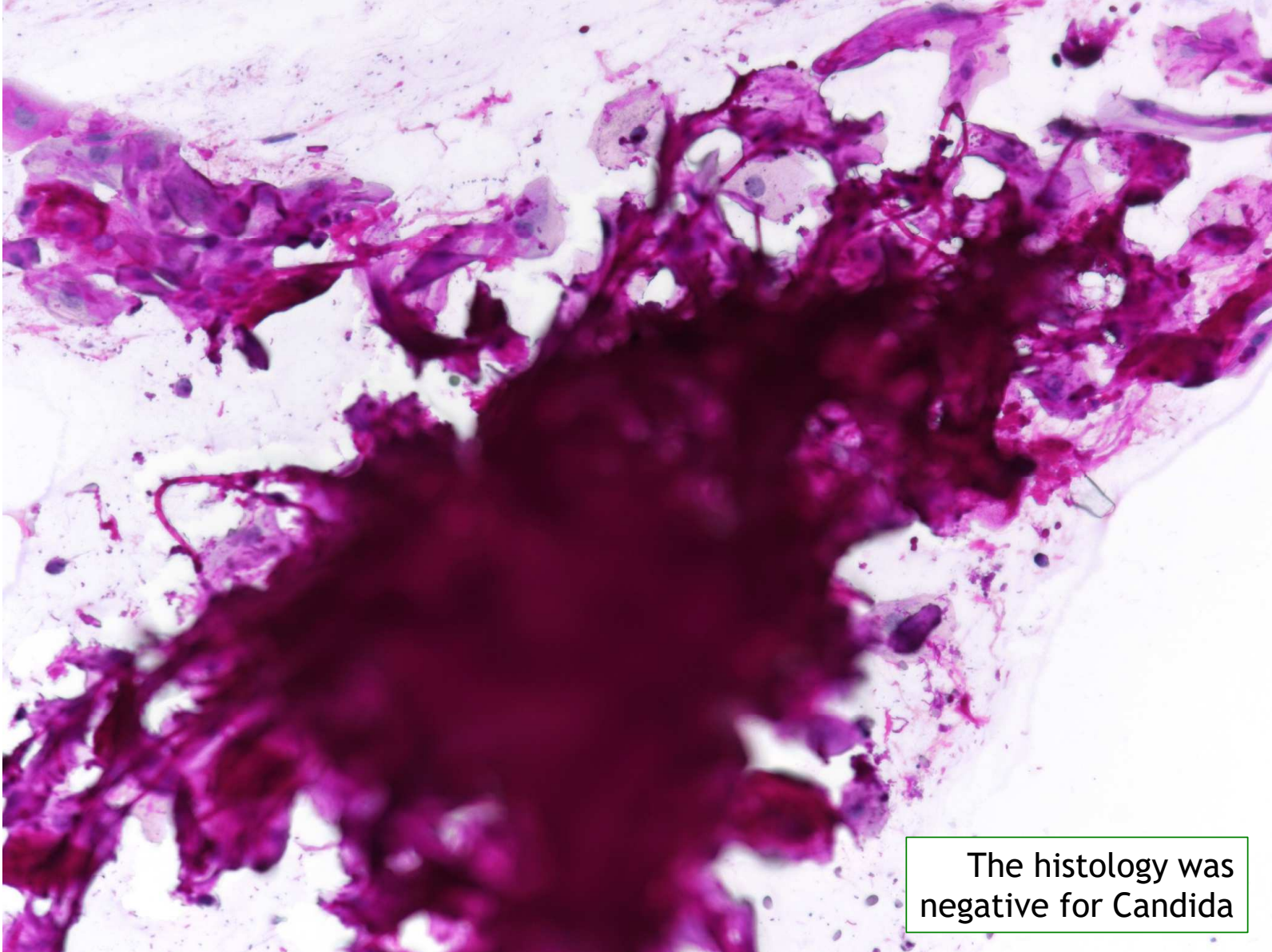
- ▶ PAS
- ▶ CD3
- ▶ Viral stains (HSV, CMV)











The histology was negative for Candida







The histology was negative for Candida



# What is your final diagnosis?

- ▶ Viral oesophagitis
- ▶ Eosinophilic oesophagitis
- ▶ Lymphocytic oesophagitis
- ▶ Pill's oesophagitis
- ▶ Extranodal marginal zone B-NHL (MALT lymphoma)
- ▶ None of the above





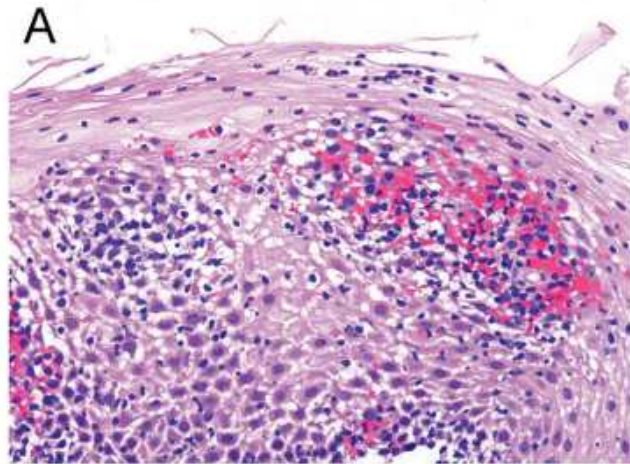
# What is the diagnosis I made?

- ▶ Candida oesophagitis (lymphocyte predominant oesophagitis, positive for Candida albicans)



# Mucosal inflammation in *Candida* esophagitis has distinctive features that may be helpful diagnostically

Isabella W. Martin<sup>1</sup> · Aaron E. Atkinson<sup>1</sup> · Xiaoying Liu<sup>1</sup> · Arief A. Suriawinata<sup>1</sup> · Joel A. Lefferts<sup>1</sup> · Mikhail Lisovsky<sup>1</sup>



**Table 1** Histologic features of inflammation in *Candida* esophagitis and reflux esophagitis

	<i>Candida</i> esophagitis, % (n = 88)	Reflux esophagitis, % (n = 64)	P-value
Basal hyperplasia	73	95	.0007
Elongated papillae	52	81	.0003
Intraepithelial neutrophils			
Total	94	22	<.0001
Band-like	75	14	<.0001
Patchy/focal	19	8	.0342
Increased intraepithelial lymphocytes			
Total	67 (59/88)	19 (12/64)	<.0001
Peripapillary	75 (44/59)	17 (2/12)	.0011
Diffuse	25 (14/59)	83 (10/12)	.0011
CD4-predominant	75 (44/59)	17 (2/12)	.005
Concurrence of intraepithelial Neutrophils and increased lymphocytes	61	2	<.0001
Concurrence of band-like neutrophils and peripapillary lymphocytes	35	0	<.0001
Concurrence of band-like neutrophils and increased CD4-predominant lymphocytes	50	0	<.0001
Co-localization of intraepithelial neutrophils and increased lymphocytes	35	2	<.0001
Intraepithelial eosinophils			
No	66	25	<.0001
Rare	20	14	<.0001
Multiple	14	39	<.0001
Erosion/ulcer	0	20	<.0001





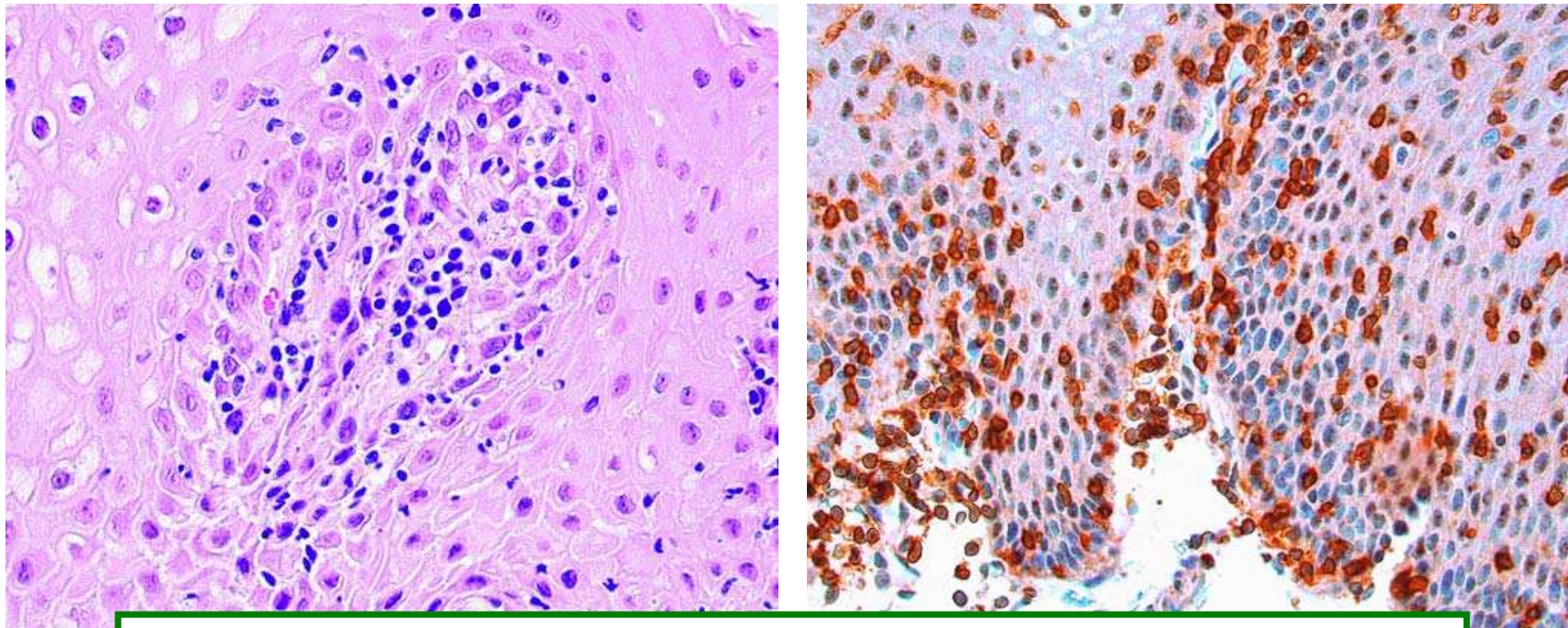
Let us talk about increased IEL counts...



## Lymphocytic Esophagitis

### A Histologic Subset of Chronic Esophagitis

*Carlos A. Rubio, MD, PhD,<sup>1</sup> Krister Sjödaahl, MD,<sup>2</sup> and Jesper Lagergren, MD, PhD<sup>2</sup>*



Increase in intraepithelial lymphocytes with peripapillary accentuation  
None (or very scarce) neutrophils, eosinophils (in low number) possible



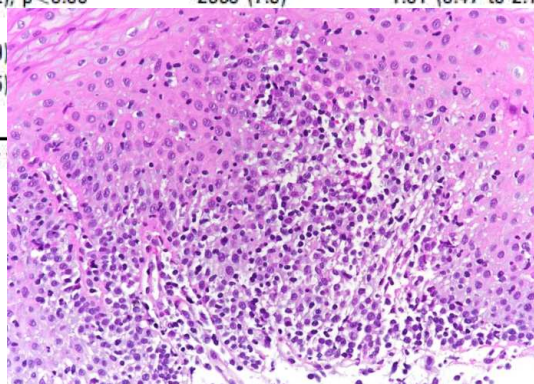
# Lymphocytic oesophagitis: clinicopathological aspects of an emerging condition

Salima Haque,<sup>1,2</sup> Robert M Genta<sup>1,2,3</sup>

**Table 1** Simultaneous gastric biopsies were available in 70 patients with LyE, 2113 patients with EoE and 31 758 with normal oesophagus; duodenal biopsies were available in 39 patients with LyE, 1052 patients with EoE and 15 007 with normal oesophagus; and ileal or colonic biopsies were available in 13 patients with LyE, 398 patients with EoE and 6095 with normal oesophagus

	Lymphocytic oesophagitis	Oesophageal eosinophilia (>15 eos/HPF)	OR (95% CI) (LyE vs EoE), probability	Normal oesophageal mucosa	OR (95% CI) (LyE vs normal), probability
<b>Demographics</b>					
Total number	119	3745	—	40654	—
Median age	63	43	p<0.001	55	p<0.001
Men	47 (39.5)	2461 (65.7)	0.34 (0.23 to 0.49), p<0.0001	14119 (31.6)	1.24 (0.86 to 1.78), ns
<b>Clinical manifestations</b>					
Dysphagia	63 (52.9)	2371 (63.3)	1.00 (0.66 to 1.51), ns	10490 (33.0)	4.97 (3.32 to 7.46), p<0.0001
GERD	22 (18.5)	707 (18.9)	0.95 (0.60 to 1.52), ns	11894 (37.4)	0.54 (0.34 to 0.85), p<0.01
Suspected EoE	37 (31.1)	2170 (57.9)	0.33 (0.22 to 0.49), p<0.0001	8379 (26.3)	1.76 (1.20 to 2.59), p<0.01
<b>Concurrent pathology</b>					
<i>Helicobacter pylori</i> gastritis (n=79)	7 (8.9)	100 (4.7)	2.16 (1.02 to 4.92), p<0.05	2330 (7.3)	1.01 (0.47 to 2.17), ns
Coeliac disease (n=39)	3 (7.7)	10 (1.0)	9.50 (2.57 to 34.9)	—	2), p<0.001
Duodenal lymphocytosis	2 (5.1)	24 (2.3)	2.60 (0.61 to 11.5)	—	4), ns
Crohn's disease	0	5 (0.2)	—	—	—

EoE, eosinophilic oesophagitis; eos, eosinophils; GERD, gastro-oesophageal reflux disease; HPF, high-power



**There is no validated cut-off value (many use >20 IEL, Carlos Rubio himself uses >40 IEL)**



## Lymphocytic oesophagitis: clinicopathological aspects of an emerging condition

Salima Haque,<sup>1,2</sup> Robert M Genta<sup>1,2,3</sup>

**Table 2** Endoscopic impressions reported in 119 patients with lymphocytic oesophagitis

Endoscopic impression	Number	%
Normal oesophagus	27	22.6
Oesophagitis	22	18.5
With suspicion of Barrett's	4	—
Eosinophilic oesophagitis	40	33.6
With rings or furrows	5	—
With whitish plaques	3	—
With stricture	6	—
Stricture	12	10.1
Motility disorder	6	5.0
Schatzki ring	3	2.5
<i>Candida</i>	2	1.6
Achalasia	1	0.8
Not reported	6	5.0

„microscopic oesophagitis“ in patients with dysphagia (also about 10-20% of patients with EOE are „negative“ upon endoscopy)

- ▶ One of 1000 (0.1%) patients who have oesophageal biopsies shows dense peripapillary lymphocytic infiltrates (“lymphocytic oesophagitis”)
- ▶ These patients present with dysphagia, odynophagia and motility disorders as commonly as patients with EoE
- ▶ In adults, lymphocytic oesophagitis affects predominantly older women and is not associated with Crohn’s disease





## Lymphocytic esophagitis: an update on histologic diagnosis, endoscopic findings, and natural history

Deepa T. Patil,<sup>1</sup> Suntrea Hammer,<sup>2</sup> Rupert Langer,<sup>3</sup> and Rhonda K. Yantiss<sup>4</sup>



**Table 1.** Comparison of endoscopic findings in lymphocytic esophagitis and eosinophilic esophagitis

Endoscopic finding	Lymphocytic esophagitis (cumulative data; n = 359) <sup>a</sup>	Eosinophilic esophagitis <sup>b</sup>
Linear furrows	9.5%	48%
Rings	18.4%	44%
Pallor/decreased vascularity	0%	41%
White plaques/exudates	3%	27%
Strictures	13%	21%
Erosive esophagitis	24%	17%
Normal	31%	17%

“Based on the current literature, esophageal lymphocytosis is a **common, nonspecific histologic finding** that may be encountered in a variety of different situations. In adults, this pattern of injury is associated with gastroesophageal reflux disease, infection, dysmotility, and immune-mediated disorders, while **in children there is a strong association with Crohn’s disease.**”

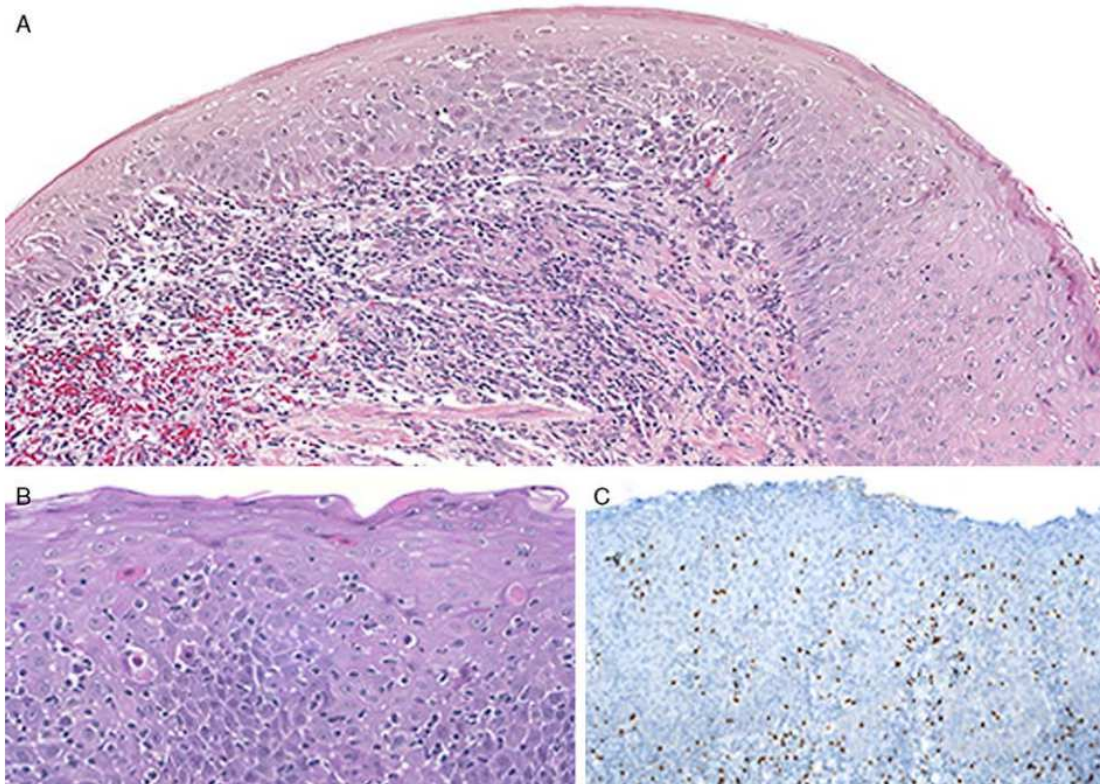
In terms of pathology report, we recommend using **lymphocytic esophagitis-pattern of injury** in the diagnostic line followed by a comment stating that this is a nonspecific histologic finding and listing the aforementioned conditions associated with this finding.”



# Lichenoid Esophagitis

## Clinicopathologic Overlap With Established Esophageal Lichen Planus

Safia N. Salaria, MD,\* Amer K. Abu Alfa, MD,\*† Michael W. Cruise, MD, PhD,\*  
 Laura D. Wood, MD, PhD,\* and Elizabeth A. Montgomery, MD\*



**FIGURE 2.** LEP. A, Dense lymphocytic infiltrate involving the lamina propria and squamous epithelium. B, Necrotic squamous cells with dense eosinophilic cytoplasm. C, FOXP3-positive T lymphocytes are present.

**TABLE 1.** Clinicopathologic Features of LPE Versus LEP

	Established LPE, % (N)	LEP, % (N)	P
No. patients	32 (21)	68 (44)	
Female	95 (20)	71 (31)	0.000001
Median age (y)	63	58	0.083
Dysphagia	43 (9)	23 (10)	NS
Strictures	38 (8)	9 (4)	0.000001
Distribution			
Mid esophagus	14 (3)	27 (12)	NS
Upper and lower esophagus	33 (7)	18 (8)	NS
Associated rheumatologic disorders	24 (5)	11 (5)	0.00236
HIV	0 (0)	14 (6)	0.00007
Viral hepatitis	0 (0)	9 (4)	< 0.05
Taking > 3 medications	67 (14)	59 (26)	0.00001
Progression to dysplasia/carcinoma	5 (1)	7 (3)	NS

NS indicates not significant.

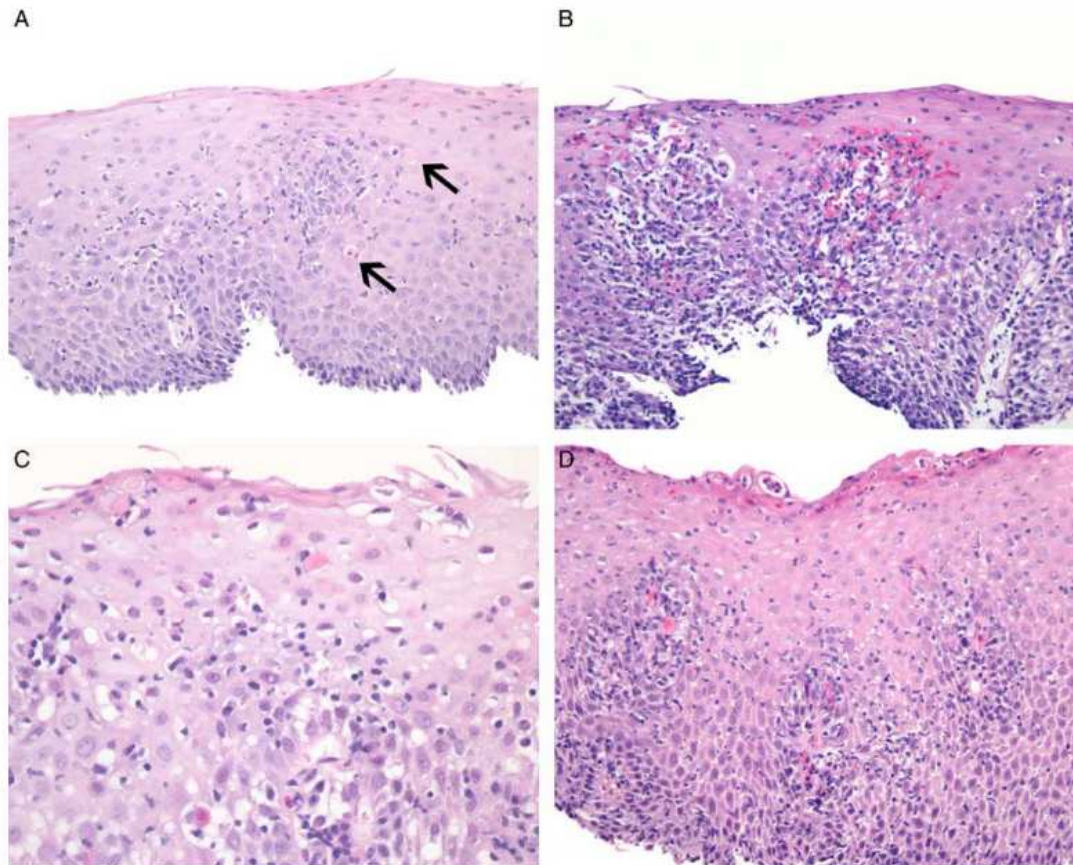




# Lymphocyte-predominant Esophagitis

## A Distinct and Likely Immune-mediated Disorder Encompassing Lymphocytic and Lichenoid Esophagitis

Meredith E. Pittman, MD,\* Erika Hisson, MD,\* Philip O. Katz, MD,† and Rhonda K. Yantiss, MD\*



**TABLE 2.** Relationships Between Clinical Features and Neutrophilia in Patients With Lymphocyte-predominant Esophagitis

Characteristics	n (%)		P
	Cases with Neutrophils (N = 16)	Cases Without Neutrophils (N = 45)	
Sex			
Male	4 (25)	13 (29)	
Female	12 (75)	32 (71)	
Mean age at diagnosis (y)	47	59	
Common presenting symptoms			
Dysphagia	11 (69)	23 (51)	
Abdominal pain	5 (31)	7 (16)	
Esophageal findings at endoscopy			
Normal	0 (0)	13 (29)	0.01
White flecks or plaques	6 (38)	2 (4)	0.003
Multiple rings	5 (31)	9 (20)	
Edema with longitudinal furrows	0 (0)	6 (13)	
Ulcers	3 (19)	1 (2)	0.05
Diffuse mucosal nodularity	4 (25)	1 (2)	0.015
Immune-mediated condition or immunodeficiency	14 (88)	27 (60)	0.04

# Lymphocyte-predominant Esophagitis

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Meredith E. Pittman, MD,\* Erika Hisson, MD,\* Philip O. Katz, MD,† and Rhonda K. Yantiss, MD\*

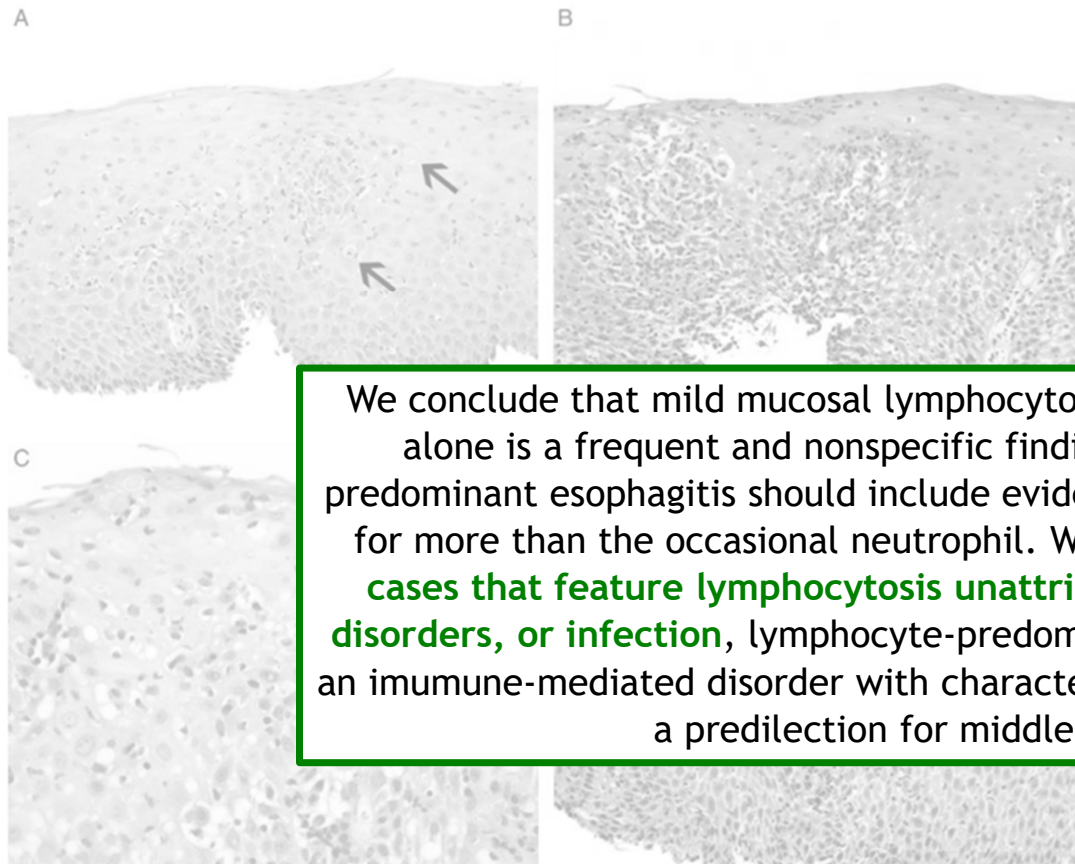


TABLE 2. Relationships Between Clinical Features and Neutrophilia in Patients With Lymphocyte-predominant Esophagitis

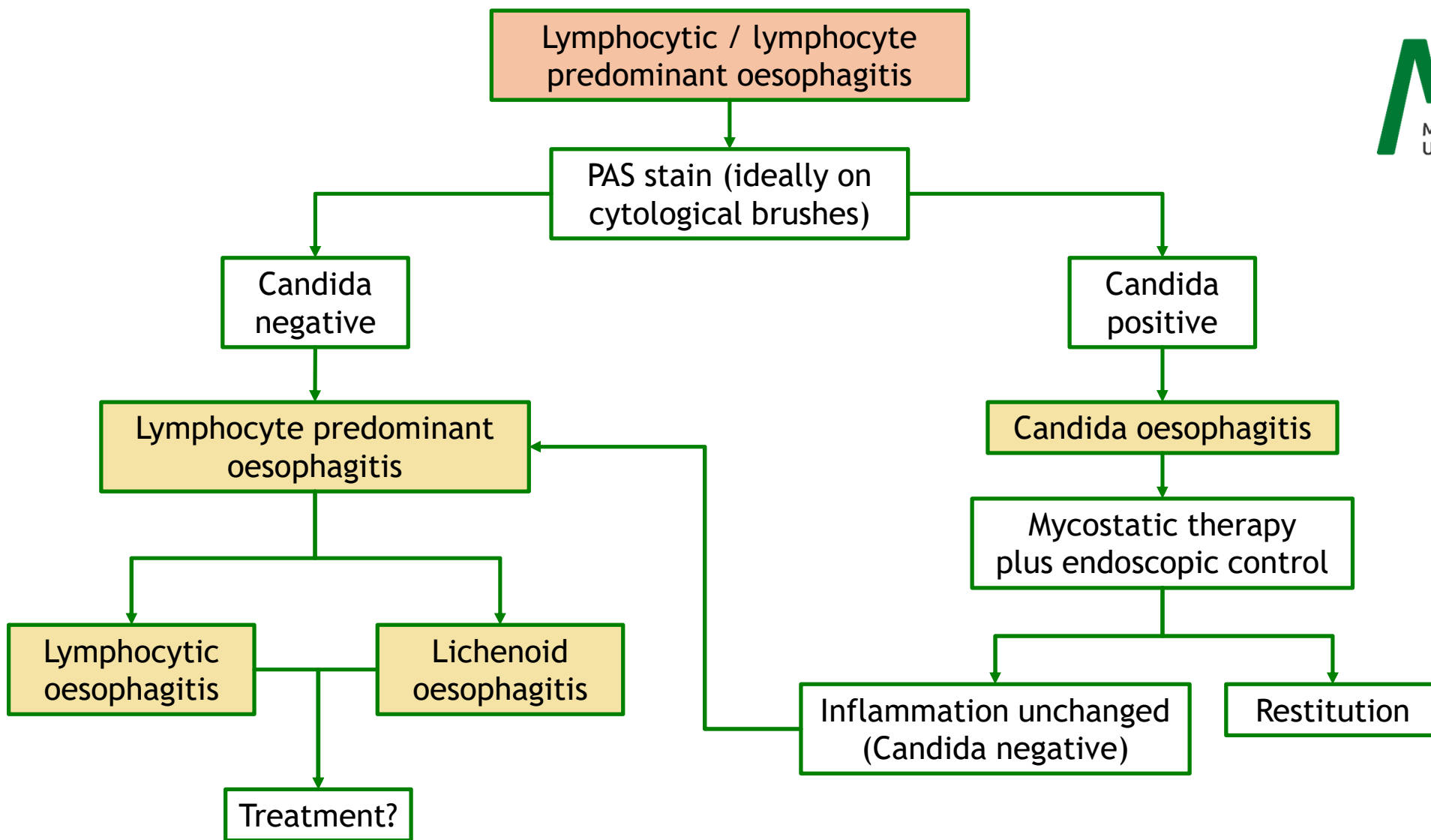
Characteristics	n (%)		P
	Cases with Neutrophils (N = 16)	Cases Without Neutrophils (N = 45)	
Sex			
Male	4 (25)	13 (29)	
Female	12 (75)	32 (71)	
		59	
		23 (51)	
		7 (16)	
		13 (29)	0.01
		2 (4)	0.003
		9 (20)	
		6 (13)	
		1 (2)	0.05
		1 (2)	0.015
		27 (60)	0.04

We conclude that mild mucosal lymphocytosis (i.e.,  $\geq 20$  lymphocytes/HPF) alone is a frequent and nonspecific finding; criteria for lymphocyte-predominant esophagitis should include evidence of mucosal injury and allow for more than the occasional neutrophil. When this diagnosis is **limited to cases that feature lymphocytosis unattributed to acid reflux, motility disorders, or infection**, lymphocyte-predominant esophagitis may represent an immune-mediated disorder with characteristic clinical manifestations and a predilection for middle-aged women

condition or immunodeficiency







# Summary

- ▶ Patients with dysphagia represent an “every-day-problem” in gastrointestinal pathology (every fourth patient is endoscopically “negative” → microscopic oesophagitis)
- ▶ The approach to patients with (severe) lymphocytic / lymphocyte predominant inflammation warrants a systematic joint effort by clinicians and pathologists
- ▶ Diagnostic categories that mainly need to be considered include Candida infection, lymphocytic oesophagitis, lichenoid oesophagitis and/or lymphocyte predominant oesophagitis



## ... coming back to our patient

- ▶ We can currently not tell, whether *Candida albicans* is the driver of the process (i.e., responsible for the inflammation) or an innocent passenger (i.e., a simple bystander because the patient has dysphagia and/or pain)
- ▶ Time will answer this question!





**Thank you very much for  
your kind attention!**

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